WEST Search History

DATE: Wednesday, November 12, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L16	imexon and (oil or oils)	6	L16
L15	L12 and (oil or oils)	15	L15
L14	L12 and micelle$	0	L14
L13	L12 and liposome$	1	L13
L12	cyanoaziridine	36	L12
L11	imexon	13	L11
L10	L9 and ((424/450)!.CCLS.)	1	L10
L9	azimexon and liposome$	52	L9
L8	azimexon and micelle$	3	L8
L7	azimexon same micelle$	0	L7
L6	azimexon same liposome$	2	L6
L5	azimexon	100	L5
L4	aziridine$ and micelle$	122	L4
L3	aziridine$ same micelle$	0	L3
L2	aziridine$ same liposome$	1	L2
L1	aziridine	7579	L1

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Search Results - Record(s) 1 through 1 of 1 returned.

☑ 1. Document ID: US 4275000 A

L2: Entry 1 of 1 File: USPT Jun 23, 1981

US-PAT-NO: 4275000
DOCUMENT-IDENTIFIER: US 4275000 A

TITLE: Peptide macromolecular complexes

DATE-ISSUED: June 23, 1981

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ross; Walter C. J.	Sunbury on Thames			GB2

US-CL-CURRENT: 530/359; 424/179.1, 435/188, 530/363, 530/386, 530/389.6, 530/391.9, 530/395, 530/403, 530/404, 530/405, 530/406, 530/408, 530/409, 530/410, 530/825, 530/866

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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Terms	Documents
aziridine$ same liposome$	1

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Previous Page Next Page

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L10: Entry 1 of 1 File: USPT Dec 18, 2001

DOCUMENT-IDENTIFIER: US 6331289 B1
TITLE: Targeted diagnostic/therapeutic agents having more than one different vectors

Brief Summary Text (8):
There is a limited body of prior art relating to targeted ultrasound contrast agents. Thus, for example, US-A-5531980 is directed to systems in which the reporter comprises an aqueous suspension of air or gas microbubbles stabilised by one or more film-forming surfactants present at least partially in lamellar or laminar form, said surfactant(s) being bound to one or more vectors comprising "bioactive species designed for specific targeting purposes". It is stated that the microbubbles are not directly encapsulated by surfactant material but rather that this is incorporated in liquid-filled liposomes which stabilise the microbubbles. It will be appreciated that lamellar or laminar surfactant material such as phospholipids present in such liposomes will inevitably be present in the form of one or more lipid bilayers with the lipophilic tails "back-to-back" and the hydrophilic heads both inside and outside (see e.g. Schneider, M. on "Liposomes as drug carriers: 10 years of research" in Drug targeting, Nyon, Switzerland, 3-5 October 1984, Buri, P. and Gumma, A. (Ed), Elsevier, Amsterdam 1984).

Brief Summary Text (10):
WO-A-9320802 proposes that tissue-specific ultrasonic image enhancement may be achieved using acoustically reflective oligolamellar liposomes conjugated to tissue-specific ligands such as antibodies, peptides, lectins etc. The liposomes are deliberately chosen to be devoid of gas and so will not have the advantageous echogenic properties of gas-based ultrasound contrast agents. Further references to this technology, e.g. in targeting to fibrin, thrombi and atherosclerotic areas are found in publications by Alkanonyuksel, H. et al. in J. Pharm. Sci. (1996) 85(5), 486-490; J. Am. Coll. Cardiol. (1996) 27(2) Suppl A, 298A; and Circulation, 68 Sci. Sessions, Anaheim 13-16 November 1995.

Detailed Description Text (13):
The reporter may be made by any convenient process, for example by making gas-containing or gas-generating formulations. Representative examples include the preparation of a suspension of gas microbubbles by contacting a surfactant with gas and mixing them in the presence of an aqueous carrier, as described in WO 9115244; or by atomising a solution or dispersion of a wall-forming material in the presence of a gas in order to obtain hollow microcapsules, as described in EP 512693A1; preparation of solid microspheres by a double emulsion process, as described in U.S. Pat. No. 5,648,095; or a process for forming hollow microcapsules by spray-drying as described in EP 681843A2; or preparing gas-filled liposomes by shaking an aqueous solution comprising a lipid in the presence of a gas as described in U.S. Pat. No. 5,469,854.

Detailed Description Text (55):
The major mechanism for uptake of particles by the cells of the reticuloendothelial system (RES) is opsonisation by plasma proteins in blood; these mark foreign particles which are then taken up by the RES. The biological properties of PEG spacer elements used in accordance with the invention may serve to increase contrast agent circulation time in a similar manner to that observed for PEGylated liposomes (see e.g. Klibanov, A. L. et al. in FEBS Letters (1990) 268, 235-237 and Blume, G. and Cevc, G. in Biochim. Biophys. Acta (1990) 1029, 91-97).

Detailed Description Text (144):

abamectin, abundiazole, acaprazine, acabrose, acebrochol, aceburic acid, acebutolol, acecainide, acecarbromal, aceclidine, aceclofenac, acedapsone, acediasulfone, acedoben, acefluranol, acefurtiamine, acefylline clofibrol, acefylline piperazine, aceglatone, aceglutamide, aceglutamide aluminium, acemetacin, acenocoumarol, aceperone, acepromazine, aceprometazine, acequinoline, acesulfame, acetaminophen, acetaminosalol, acetanilide, acetarsone, acetazolamide, acetergamine, acetiamine, acetiromate, acetohexamide, acetohydroxamic acid, acetomeroctol, acetophenazine, acetorphine, acetosulfone, acetriozate, acetryptine, acetylcholine chloride, acetylcolchinol, acetylcysteine, acetyldigitoxin, acetylleucine, acetylsalicyclic acid, acevaltrate, acexamic acid, acifran, acipimox, acitemate, acitretin, acivicin, aclantate, aclarubicin, aclatonium napadisilate, acodazole, aconiazide, aconitine, acoxatrine, acridorex, acrihellin, acrisorcin, acrivastine, acrocinide, acronine, actinoquinol, actodigin, acyclovir, adafenoxate, adamexine, ademetionine, adenosine phosphate, adibendan, adicillin, adimolol, adinazolam, adiphenine, aditeren, aditoprim, adrafinil, adrenalone, afloqualone, afurolol, aganodine, ajmaline, aklomide, alacepril, alafosfalin, alanine mustard, alanosine, alaproclate, alazanine triclofenate, albendazole, albendazole oxide, albuterol, albutoin, alclofenac, alcometasone dipropionate, alcloxa, alcuronium chloride, aldioxa, aldosterone, alepride, aletamine, alexidine, alfacalcidol, alfadex, alfadolone, alfaprostol, alfaxalone, alfentanil, alfuzosin, algestone acetonide, algestone acetophenide, alibendol, aliconazole, alifedrine, aliflurane, alimadol, alinidine, alipamide, alitame, alizapride, allantoin, alletorphine, allobarbital, alloclamide, allocupreide, allomethadione, allopurinol, allylestrenol, allyl isothicyanate, allylprodine, allylthiourea, almadrate sulfate, almasilate, almecillin, almestrone, alminoprofen, almitrine, almoxatone, alonacic, alonimid, aloxistatin, alozafone, alpertine, alphacetylmethadol, alphameprodine, alphamethadol, alphaprodine, alpha-vinylaziridinoethyl acetate, alpidem, alpiropride, alprazolam, alprenolol, alprostadil, alrestatin, altanserin, altapizone, alteconazole, althiazide, altrenogest, altretamine, aluminium acetate, aluminium clofibrate, aluminium subacetate, alverine, amadinone acetate, amafolone, amanozine, amantadine, amantanium bromide, amantocillin, ambasilide, ambazone, ambenonium chloride, ambenoxan, ambroxol, ambruticin, ambucaine, ambucetamide, ambuphylline, ambuside, ambutonium bromide, amcinafal, amcinafide, amcinonide, amdinocillin, amdinocillin pivoxil, amebucort, amedalin, ametantrone, amezepine, amezinium metilsulfate, amfenac, amfepentorex, amfetaminil, amflutizole, amfonelic acid, amicarbalide, amicibone, amicloral, amicycline, amidantel, amidapsone, amidephrine, amiflamine, amifloverine, amifloxacin, amifostine, amikacin, amikhelline, amiloride, aminacrine, amindocate, amineptine, aminobenzoic acid, aminocaproic acid, aminoethyl nitrate, aminoglutethimide, aminohippuric acid, aminometradine, aminopentamide, aminophylline, aminopromazine, aminopterin, aminopyrine, aminoquinol, aminoquinuride, aminorex, aminosalicyclic acid, aminothiadiazole, aminothiazole, amiodarone, amiperone, amipheazole, amipizone, amiprilose, amiquinsin, amisometradine, amisulpride, amiterol, amithiozone, amitraz, amitriptyline, amitriptylinoxide, amixetrine, amlexanox, amlodipine, amobarbital, amodiaquine, amogastrin, amolanone, amonofide, amoproxan, amopyroquin, amorolfine, amocanate, amosulalol, amotriphene, amoxapine, amoxecaine, amoxicillin, amoxydramine camsilate, amperozide, amphecloral, amphenidone, amphetamine, amphotalide, amphotericin B, ampicillin, ampiroxicam, amprolium, ampyrimine, ampyzine, amquinate, amrinone, amsacrine, amygdalin, amylene, amylmetacresol, amyl nitrite, anagestone acetate, anagrelide, anaxirone, anazocine, anazolene, ancarolol, ancitabine, androstanediol, androstanol propionate, androstenetrione, androstenonol propionate, anethole, anguidine, anidoxime, anilamate, anileridine, aniline, anilopam, anipamil, aniracetam, anirolac, anisacril, anisindione, anisopirol, anisoylbromacrylic acid, anitrazafen, anpirtoline, ansoxetine, antafenite, antazoline, antazonite, anthelmycin, anthiolimine, anthralin, anthramycin, antienite, antimony potassium tartrate, antimony thioglycollate, antipyrine, antrafenine, apalcillin, apazone, apicycline, apomorphine, apovincamine, apraclonidine, apramycin, aprindine, aprobarbital, aprofene, aptazapine, aptocaine, arabinosylmercaptopurine, aranotin, arbaprostil, arbekacin, arclofenin, arfendazam, arginine, arginine glutamat, arildone, arnolol, aronixil, arotinolol, arpinocid, arpromidine, arsanilic acid, arsthinol, artemisinin, articaine, asaley, ascorbic acid, ascorbyl palmitate, asocainol, aspartame, aspartic acid, asperlin, aspoxicillin, astemizole, atamestane, atenolol, atipamezole, atiprosin, atolide, atracurium besilate, atromepine, atropine, atropine oxide, auranofin, aurothoiglucose, aurothioglycanide, avilamycin-A, avridine, axamozide, azabon,

azabuperone, azacitodine, azaclorzine, azaconazole, azacosterol, azacyclonol, azaftozine, azaguanidine, azaloxan, azamethonium bromide, azamulin, azanator, azanidazole, azaperone, azapicyl, azaprocin, azaquinzole, azaribine, azarole, azaserine, azaspirium chloride, azastene, azastrptonigrin, azatodine, azathioprine, azauridine, azelastine, azepexole, azepindole, azetepa, azidamfenicol, azidocillin, azimexon, azintamide, azipramine, azithromycin, azlocillin, azolimine, azosemide, azotomycin, aztreonam, azumolene, bacampicillin, baclofen, bacmecillinam, balsalazide, bamaluzole, bambuterol, bamethan, bamifylline, bamipine, bamnidazole, baquiloprim, barbexaclone, barbital, barucainide, batilol, bazinaprine, becanthone, beclamide, beclobrate, beclomethasone dipropionate, beclotiamine, befiperide, befunolol, befuraline, bekanamycin, belarizine, beloxamide, bemarinone, bemegride, bemetizide, bemitradine, benactyzine, benafentrine, benanserin, benapryzine, benaxibine, benazepril, bencianol, bencisteine, benclonidine, bencyclane, bendamustine, bendazac, bendazol, benderizine, bendroflumethiazide, benethamide penicillin, benexate, benflorex, benfosformin, benfotiamine, benfurodil hemisuccinate, benhepazone, benidipine, benmoxin, benolizime, benorilate, benorterone, benoxafos, benoxaprofen, benoxinate, benperidol, benproperine, benrixate, bensalan, benserazide, bensuldazic acid, bentazepam, bentemazole, bentiamine, bentipimine, bentiromide, benurestat, benzaldehyde, benzalkonium chloride, benzaprinoxide, benzarone, benzbromarone, benzestrol, benzethidine, benzethonium chloride, benzetimide, benzilonium bromide, benzindopyrine, benziodarone, benzmalecene, benznidazole, benzobarbital, benzocaine, benzoclidine, benzoctamide, benzodepa, benzododecinium chloride, benzoic acid, benzoin, benzonatate, benzopyrronium bromide, benzoquinium chloride, benzotript, benzoxiquine, benzoxonium chloride, benzoyl peroxide, benzoylpas, benzphetamine, benzpiperylon, benzpyrinium bromide, benzquercin, benzquinamide, benzthiazide, benztropine, benzydamine, benzylpenicillin, benzylsulfamide, beperidium iodide, bephenium naphtoate, bepiastine, bepridil, beraprost, berberine sulfate, bermastine, bermoprofen, berythromycin, besulpamide, beslunide, beta carotene, betacetylmethadol, betahistine, betaine, betameprodine, betamethadol, betamethasone, betamethasone acetate, betamethasone acibutate, betamethasone benzoate, betamethasone dipropionate, betamethasone phosphate, betamethasone valerate, betamicin, betaprodine, betaxolol, betazole, bethanechol chloride, bethanidine, betiatide, betoxycaine, bevantolol, bevonium metilsulfate, bezafibrate, bezitramide, bialamicol, bibenzonium bromide, bibrocathol, bicifadine, biclodil, biclofibrate, biclotymol, bicozamycin, bidimazium iodine, bietamiverine, bietaserpine, bifemelane, bifepramide, bifluranol, bifonazole, binedaline, binfloxacin, binfibrate, bioallethrin, bioresmethrin, biotin, bipenamol, biperiden, biphenamine, biriperone, bisacodyl, bisantrene, bis(aziridinyl) butanediol, bisbendazole, bisbentiamine, bisfenazone, bisfentidine, bismuth betanaphthol, bismuth-triglycollamate, bismuth subgallate, bismuth subsalicylate, bisorbin, bisoprolol, bisorcic, bioxatin acetate, bispyrithione magsulfex, bithionol, bithionoloxide, bitipazone, bitoterol, bitoscantate, bleomycin, bluensomycin, bofumustine, bolandiol dipropionate, bolasterone, bolazine, boldenone undecylenate, bolenol, bolmantalate, bometolol, bopindolol, bornaprine, bornaprolol, bornelone, botiacrine, boxidine, brallobarbital, brazergoline, brefonalol, bremazocine, brequinar, bretylium tosylate, brindoxime, brivundine, brobactam, broclepride, brocresine, brocrinat, brodimoprim, brofaromine, brofezil, brofoxine, brolaconazole, brolamfetamine, bromacrylide, bromadoline, bromamid, bromazepam, bromchlorenone, bromebric acid, bromerguride, brometenamine, bromfenac, bromhexine, bromindione, bromisovalum, bromociclen, bromocriptine, bromodiphenhydramine, bromofenofos, bromopride, bromoxandide, bromperidol, bromperidol decanoate, brompheniramine, bronopol, broparestrol, broperamole, bropirimine, broquinaldol, brosotamide, brosuximide, brotianide, brotizolam, brovanexine, brovincamine, broxaldine, broxaterol, broxitalamic acid, broxuridine, broxyquinoline, bruceantin, brucine, bucainide, bucetin, buciclovir, bucillamine, bucindolol, bucladesine, buclizine, buclosamide, bucloxic acid, bucolome, bucricaine, bucromarone, bucrylate, bucumolol, budesonide, budipine, budotitane, budralazine, bufenadrine, bufeniode, bufetolol, bufexamac, bufezolac, buflomedil, bufogenin, buformin, bufrolin, bufuralol, bumadizone, bumecaine, bumepidil, bumetanide, bumetrizole, bunaftine, bunamidine, bunamiodyl, bunaprolast, bunazosin, bunitrolol, bunolol, buparvaquone, bupicomide, bupivacaine, bupranolol, buprenorphine, bupropion, buquineran, buquinolate, buquiterine, buramate, burodiline, buspirone, busulfan, butabarbital, butacaine, butacetin, butaclamol, butadiazamide, butafosfan, butalamine, butalbital, butamben, butamirate, butamisole, butamoxane, butanediol cyclic sulfite, butanilicaine, butanixin, butanserin, butantrone, butaperazine, butaprost, butaverine, butedronate,

buterizine, butetamate, butethamine, buthiazide, butibufen, butidrine, butikacin, butilfenin, butinazocine, butinoline, butirosin, butixirate, butobendine, butoconazole, butocrolol, butoctamide, butofilolol, butonate, butopamine, butopiprine, butoprozine, butopyrammonium iodide, butorphanol, butoxamine, butoxylate, butriptyline, butropium bromide, butylated hydroxyanisole, butylated hydroxytoluene, butylparaben, butynamine, buzepide metiodide, cabastine, cabergoline, cadralazine, cafaminol, cafedrine, caffeine, calcifediol, calcitrol, calcium citrate, calcium dobesilate, calcium glubionate, calcium gluceptate, calcium gluconate, calcium glycerophosphate, calcium hypophosphite, calcium lactate, calcium lactobionate, calcium levulinate, calcium mandelate, calcium pantothenate, calcium phosphate dibasic, calcium phophate tribasic, calcium saccharate, calcium stearate, calusterone, camazepam, cambendazole, camiverine, camostast, camphotamide, camptothecin, camylofin, canbisol, cannabinol, canrenoic acid, canrenone, cantharidine, capobenic acid, capreomycin, caproxamine, capsaicine, captamine, captodiame, captopril, capuride, caracemide, caramiphen, carazolol, carbachol, carbadox, carbaldrate, carbamazepine, carbamide peroxide, carbantel lauryl sulfate, carbaril, carbarsone, carbaspirin calcium, carbazeran, carbazochrome, carbazachrome salicylate, carbazachrome sulfonate, carbazocine, carbeniciltin, carbenicillin indanyl, carbencillin phenyl, carbenoxolone, carbenzide, carbestrol, carbetapentane, carbidopa, carbimazole, carbinoxamine, carbiphene, carbocloral, carbocysteine, carbofenotion, carbol-fuschin, carbomycin, carboplatin, carboprost, carboprost methyl, carboquone, carbromal, carbubarb, carburazepam, carbutamide, carbuterol, carcainium chloride, carebastine, carfentanil, carfimate, carisoprodol, carmantadine, carmetizide, carmofur, carmustine, carnidazole, carnitine, carocainide, caroverine, caroxazone, carperidine, caperone, carphenazine, carpindolol, carpiramine, carprofen, carpronium chloride, carsalam, cartazolate, carteolol, carubicin, carumonam, carvedilol, carzenide, carzolamide, cathine, cathinone, cefaclor, cefadroxil, cefalonium, cefaloram, cefamandole, cefamandole naftate, cefaparole, cefatrizine, cefazaflur, cefazedone, cefazolin, cefbuperazone, cefcanel, cefcanel daloxate, cefedrolor, cefempidone, cefepime, cefetamet, cefetrizole, cefvitril, cefixime, cefmenoxime, cefmepidium chloride, cefmetazole, cefminox, cefodizime, cefonizid, cefoperazone, ceforanide, cefotaxime, cefotetan, cefotiam, cefoxazole, cefoxitin, cefpimizole, cefpiramide, cefpirome, cefpodoxime, cefpodoxime proxetil, cefquinome, cefrotil, cefroxadine, cefsulodin, cefsumide, ceftazidime, cefteram, ceftezole, ceftiofur, ceftiolene, ceftioxide, ceftizoxime, ceftriaxone, cefuracetime, cefuroxime, cefuraxime axetil, cefurzonam, celiprolol, cephacetrile, cephalexin, cephaloglycin, cephaloridine, cephalothin, cephapirin, cephradine, cetaben, cetamolol, cethexonium chloride, cetiedil, cetirizine, cetocycline, cetohexazine, cetophenicol, cetotiamine, cetoxime, cetraxate, chaulmosulfone, chendiol, chiniofon, chlophedianol, chloracyzine, chloral betaine, chloral hydrate, chloralose, chlorambucil, chloramine, chloramphenicol, chloramphenicol palmitate, chloramphenicol succinate, chlorazanil, chlorbenzoxamine, chlorbetamide, chlorcyclizine, chlordantoin, chlordiazepoxide, chlordimorine, chlorhexadol, chlorhexidine, chlorhexidine phosphanilate, chlorindanol, chlorisondamine chloride, chlormadinone acetate, chlormerodrin, chlormezanone, chlormidazole, chloronaphazine, chloroazodin, chlorobutanol, chlorocresol, chlorodihydroxyandrostenone, chloroethyl mesylate, 5-chloro-3'-fluoro-2'3-dideoxyuridine, chloroguanide, chlorophenothane, chloroprednisone acetate, chloroprocaine, chloropyramine, chloroquine, chloroserpidine, chlorothen, chlorothiazide, chlorotriansene, chloroxine, chloroxylenol, chlorozotocin, chlorphenesin, chlorphenesin carbamate, chlorpheniramine, chlorphenoctium amsonate, chlorphenoxamine, chlorphentermine, chlorproethazine, chlorproguanil, chlorpromazine, chlorpropamide, chlorprothixene, chlorquinaldol, chlortetracycline, chlorthalidone, chlorthenoxazine, chlorzoaxazone, chloecalciferol, cholic acid, choline chloride, choline glycerophosphate, chromocarb, chromonar, ciadox, ciamexon, cianergoline, cianidol, cianopramine, ciapilome, cicaprost, cicarperone, ciclactate, ciclafrine, ciclazindol, cicletanine, ciclomenol, ciclonicate, ciclonium bromide, ciclopirox, ciclopramine, cicloprofen, cicloprolol, ciclosidomine, ciclotizolam, ciclotropium bromide, cicloxilic acid, cicloxolone, cicortonide, cicrotic acid, cidoxepin, cifenline, cifostodine, ciglitazone, ciheptolane, ciladopa, cilastatine, cilazapril, cilazaprilat, cilobamine, cilofungin, cilostamide, cilostazol, ciltoprazine, cimaterol, cimemoxin, cimepanol, cimetidine, cimetropium bromide, cimoxatone, cinchonine, cinchophen, cinecromen, cinepaxadil, cinepazet, cinepazic acid, cinepazide, cinfenine, cinfenoac, cinflumide, cingestol, cinitapride, cinmetacin, cinnamaverine, cinnamedrine, cinnarizine, cinnarizine clofibrate, cinnofuradione, cincotramide, cinodine, cinolazepam, cinoquidox,

cinoaxin, cinoxate, cinoxolone, cinooxopazide, cinperene, cinprazole, cinpropazide, cinromide, cintazone, cintriamide, cinperone, ciprafamide, ciprafazone, ciprefadol, ciprocinonide, ciprofibrate, ciprofloxacin, cipropride, ciproquazone, ciprostene, ciramadol, cirazoline, cisapride, cisconazole, cismadinone, cisplatin, cistinexine, citalopram, citatepine, citenamide, citenazone, citicoline, citiolone, clamidoxic acid, clamoxyquin, clanfenur, clanobutin, clantifen, clarithromycin, clavulanic acid, clazolam, clazolimine, clazuril, clebopride, clefamide, clemastine, clemeprol, clemizole, clenbuterol, clenpirin, cletoquine, clibucaine, clidafidine, clidanac, clidinum bromide, climazolam, climbazole, climiqualine, clindamycin, clindamycin palmitate, clindamycin phosphate, clinofibrate, clinolamide, cliquinol, clioxanide, clipoxamine, cliprofen, clobazam, clobenoside, clobenzepam, clobenzorex, clobenztropine, clobetasol propionate, clobetasone butyrate, clobutinol, clobuzarit, clocanfamide, clocapramine, clociguanil, clocinizine, clocortolone acetate, clocortolone pivalate, clocoumarol, clodacaine, clodanolene, clodazon, clodoxopone, clodronic acid, clofazimine, clofenamic acid, clofenamide, clofenciclan, clofenetamine, clofenoxyde, clofenvinfos, clofeverine, clofexamide, clofezone, clofibrate, clofibric acid, clofibride, clofilium phosphate, cloflucarban, clofoctol, cloforex, clofurac, clogestone acetate, cloguanamil, clomacran, clomegestone acetate, clometacin, clometherone, clomethiazole, clometocillin, clomifenoxide, clominorex, clomiphene, clomipramine, clomocycline, clomoxir, clonazepam, clonazoline, clonidine, clonitazene, clonitrate, clonixeril, clonixin, clopamide, clopenthixol, cloperastine, cloperidone, clopidogrel, clopidol, clopimozide, clopipazan, clopirac, cloponone, cloprednol, cloprostenol, cloprothiazole, cloquinate, cloquinozine, cloracetadol, cloranolol, clorazepate, clorethate, clorexolone, clorgiline, cloricromen, cloridarol, clorindanic acid,

Detailed Description Paragraph Table (3):
Biotinylation agents Agent Reactivity Comments biotin-BMCC --SH biotin-DPPE* preparation of biotinylated liposomes biotin-LC-DPPE* preparation of biotinylated liposomes biotin-HPDP --SH disulphide linker biotin-hydrazide carbohydrate biotin-LC-hydrazide carbohydrate iodoacetyl-LC-biotin --NH.sub.2 NHS-iminobiotin --NH.sub.2 reduced affinity for avidin NHS-SS-biotin --NH.sub.2 disulphide linker photoactivatable biotin nucleic acids sulfo-NHS-biotin --NH.sub.2 water-soluble sulfo-NHS-LC-biotin --NH.sub.2 Notes: DPPE = dipalmitoylphosphatidylethanolamine; LC = long chain

Current US Cross Reference Classification (2):
424/450

L15: Entry 3 of 15 File: USPT Feb 26, 1991

DOCUMENT-IDENTIFIER: US 4996219 A
TITLE: Imidazolidine derivatives as immunosuppressives

Brief Summary Text (32):
Compounds of general formula XII can be prepared by reacting a cyanoaziridine of the general formula: ##STR11## in which R.sub.1, R.sub.2 and R.sub.3 have the above-given meanings, with two equivalents of an acid of the general formula:

Brief Summary Text (39):
For the preparation of pharmaceutical compositions, the compounds according to the present invention are mixed in known manner with appropriate pharmaceutical carrier substances, possibly granulated and pressed, for example into tablets or dragee cores. Filling the mixture into hard capsules is also possible. With the addition of appropriate adjuvant materials, there can also be produced a solution or suspension in water, an oil, such as olive oil, or a high molecular weight polymer, such as polyethylene glycol, and administered as injection solutions, soft gelatine capsules, syrups or drops.

Detailed Description Text (16):
A solution of 6 g. (37.8 mmol) 1-benzyl-2-cyanoaziridine in 30 ml. 6N hydrochloric acid is stirred for 1 hour at ambient temperature. Subsequently, the precipitate formed is filtered off with suction and successively washed with a little cold water, isopropanol and diethyl ether and dried in a desiccator to give 5.4 g. (62% of theory) of 2-benzylamino-3-chloropropionitrile hydrochloride; m.p. 161.degree.-162.degree. C.

L16: Entry 5 of 6 File: USPT Nov 29, 1994

DOCUMENT-IDENTIFIER: US 5369119 A
TITLE: Use of imexon as an immune suppressive and pharmaceutical compositions containing imexon

Abstract Text (1):
The subject of the present invention is the use of imexon for the production of pharmaceutical compositions with an immunosuppressive action. The present invention also provides pharmaceutical compositions containing imexon and further active materials.

Brief Summary Text (1):
The present invention is concerned with the use of imexon for the preparation of pharmaceutical compositions with an immunosuppressive action and is also concerned with pharmaceutical compositions containing imexon in combination with a further active material.

Brief Summary Text (2):
In particular, the present invention is concerned with the use of imexon for the preparation of pharmaceutical compositions for the treatment of autoimmune diseases, B cell and plasma cell neoplasias, lymphoblastic lymphomas, rejection reactions after tissue and organ transplants and viral and retroviral infections, for example AIDS or ARC (AIDS-related complex). In general, imexon can be used for the treatment of diseases in which a pathophysiologically increased B-lymphocyte proliferation or B-lymphocyte activation is to be observed.

Brief Summary Text (3):
Imexon, which has the systematic designation
4-imino-1,3-diazabicyclo-(3.1.0)-hexan-2-one, has the following structural formula:
##STR1##

Brief Summary Text (4):
With regard to its structure, imexon is not comparable with any other active compounds used therapeutically. The surprisingly found preferred action on B-lymphocutes also has no parallel with other previously known immunosuppressively-acting compounds.

Brief Summary Text (5):
Imexon and processes for the preparation thereof are known from U.S. Pat. No. 4,083,987. The compound is thereby described as being a cancerostatically-active therapeutic which displays immune-stimulating properties. The cancerostatic action was demonstrated on the basis of the inhibition of the tumour growth of Walker sarcoma 256 after the administration of imexon to rats. The immune-stimulating action can be deduced from experiments in which an increase of the leukocytes, as well as an increase of the number of the antibody-forming spleen cells could be observed after the administration of imexon. The pharmacological importance of imexon is, according to this U.S. Patent Specification, to be seen in the fact that imexon so strongly impairs the growth of the rapidly dividing cancer cells that, under certain circumstances, a regression of the tumours is possible. According to U.S. Pat. No. 4,083,987, the advantageous action of imexon lies in the simultaneous strengthening of the weakened immune defence system inherent in the body which accompanies the cancerostatic action.

Brief Summary Text (12):
Suprisingly, we have now found that imexon solves this problem and can be used as an advantageous immune suppressive. It specifically suppresses the B-cell proliferation or the B-cell activation. It can be advantageously used in the treatment of all diseases in which a polyclonal activation or proliferation of B-cells is of pathophysiological, symptomatic or clinical relevance.

Brief Summary Text (15):
Furthermore, we have, surprisingly, found that imexon inhibits the proliferation of B-lymphocytes in a dosage-dependent manner.

Brief Summary Text (16):
Thus, according to the present invention, imexon specifically suppresses pathological B-cell proliferation or B-cell activation, and this is accomplished without adverse influence on T-cell proliferation or activation.

Brief Summary Text (17):
Imexon can be used itself directly or in the form of physiologically acceptable addition salts.

Brief Summary Text (19):
The immune suppressive action of imexon could be demonstrated on the basis of the inhibition of the proliferation of human B-lymphocytes, the proliferation being induced experimentally by the B-cell growth factor (BCGF).

Brief Summary Text (20):
Furthermore, the pharmacological properties of imexon could be characterised by concanavalin A (ConA)-induced proliferation of murine splenocytes (LTT), by phythaemagglutinin (PHA)-induced proliferation of human lymphocytes, as well as by tumour growth inhibition assay (TGI).

Brief Summary Text (22):
Imexon now suppresses this procedure specifically insofar as the concanavalin A (ConA)- and phytohaemagglutinin (PHA)-induced lymphocyte proliferation, as well as the spontaneous proliferation of methylcholanthrene-induced fibrosarcoma cells (MethA), are not influenced or only in the case of 10 to 30 times higher concentrations.

Brief Summary Text (23):
The antiretroviral action of imexon could be demonstrated on the basis of the Rauscher virus leukaemia model (cf. Example 5). The influence of imexon on the spontaneous formation of lymphomas and the synthesis of antinuclear autoantibodies in the mouse (Example 6) proves the effectiveness on an animal model for autoimmune diseases.

Brief Summary Text (24):
Imexon can also be used as a combination preparation with other immune suppressives, for example cyclosporin A, ciamexon or azathioprine, as well as antiretrovirally-active substances, for example azidothymidine (AZT).

Brief Summary Text (25):
A combination of imexon with cytostatics is also possible, for example with cis-platinum complexes, such as cis-diaminodichloroplatinum, or with adriamycin, cyclophosphamide, vincristin, tamoxifen, methotrexate or 5-fluorouracil and the like. In this connection, the use of such combination preparations is of especial interest subsequent to a plasmaphaeresis for the monitoring of autoimmune diseases.

Brief Summary Text (27):
For the preparation of pharmaceutical agents, imexon is mixed in known manner with appropriate pharmaceutical carrier substances, possibly granulated and pressed, for example, into tablets or dragee cores. A filling of the mixture into hard capsules is also possible. With the addition of appropriate adjuvants, a solution or suspension in water, an oil, for example olive oil, or a high molecular weight polymer, for example polyethylene glycol, can also be produced and administered in the form of injection solutions, soft gelatine capsules, syrups or drops.

Brief Summary Text (29):
The dosage of the active material imexon depends upon the age and sex of the individual, as well as upon the nature of the indications to be treated.

Brief Summary Text (30):
In principle, the treatment can be based on the fact that 0.1 to 100 mg. of imexon per kg. body weight can be administered daily orally, intravenously, subcutaneously or intramuscularly. However, it is preferred to use amounts of from 5 to 50 mg./kg. body weight and especially 5 to 20 mg./kg. body weight. The dosages of the active material can be administered 1 to 3 times daily.

Detailed Description Text (1):
The specific immunosuppressive action of imexon is demonstrated by the following Examples:

Detailed Description Text (8):
Spleen cells (4.times.10.sup.5) of CB6F.sub.1 mice were incubated for a total of 48 hours with 0.5 .mu.g./ml. ConA in microtitre plates (Nunc GmbH, Wiesbaden, Federal Republic of Germany) and various concentrations of imexon in 6 fold batches. 5 hours before the termination of the incubation period, the cultures were pulsed with [.sup.3 H]-thymidine and subsequently harvested on glass fibre filter platelets by means of a multi-sample harvester (Skatron A. S., Lier, Norway). The filter platelets were dried and the radioactivity was determined in a Packard scintillation spectrometer.

Detailed Description Text (11):
1 ml. of human whole blood was diluted with 500 .mu.g. PHA solution (500 .mu.g./ml.) and diluted with 48 ml. DMEM medium. 200 .mu.l. amounts of this batch were mixed with 20 .mu.l. of the imexon concentration to be tested in 6 fold batches and incubated for 4 days. After pulsing with [.sup.3 H]-thymidine, incubation was continued for a further 24 hours, followed by harvesting and evaluation as described in Example 2.

Detailed Description Text (15):
1.times.10.sup.4 MethA cells were incubated with the imexon concentration to be tested in DMEM medium for 48 hours. 3 hours before the end of the incubation time, pulsing was carried out with [.sup.3 H]-thymidine, followed by harvesting and evaluated as described in Example 2.

Detailed Description Text (16):
The values given in the following Table 1 show the results of a representative experiment. They are the results of the investigations with imexon in the TGI, LTT (ConA, PHA) as well as in the BCGF assay, i.e. the influence of imexon on the proliferation of the MethA sarcoma cell, T-lymphocytes and B-cells is shown. Imexon suppressed significantly and specifically the BCGF-induced B-cell proliferation at a concentration of 1 .mu.g./ml., whereas the lymphocyte proliferation induced either by ConA or PHA was only significantly inhibited at concentrations of >10 .mu.g./ml. Furthermore, the spontaneous proliferation of MethA sarcoma cells was also only significantly suppressed at >10 .mu.g./ml.

Detailed Description Text (19):
Antiretroviral action of imexon in the Rauscher virus leukaemia model

Detailed Description Text (21):
In the following Table 2 are summarised the results of the investigations. Imexon controlled the virus-caused increased weight of the spleen in the same dosage range as azidothymidine.

Detailed Description Text (23):
Action of imexon in the case of autoimmune diseases

Detailed Description Text (24):
With increasing age, the mouse strain MRL lpr/lpr develops increasingly spontaneously lymphadenoma and SLE-like symptoms, for example the synthesis of anti-nuclear autoantibodies. For the investigation of the prophylactic effect of imexon on the

development of these symptoms, 11 week old MRL mice were treated intraperitoneally once daily with the given dosages of imexon and cyclophosphamide. The number of lymphadenomas and the concentration of antinuclear antibodies were documented. In the case of the investigation of the therapeutic potency of imexon, MRL mice, after each animal had developed at least one lymphadenoma (about 14 week old animals), were also treated once daily with the given dosages of imexon and cyclophosphamide. The measurment parameters were again the number of lymphadenomas, as well as the autoantibody titre.

Detailed Description Text (25):
The results of these investigations have shown that imexon, in the case of very good compatibility, lowers the number of spontaneously arising lymphadenomas and the concentration of DNA-specific antibodies. The effectiveness of imexon was also shown in the case of therapeutic use with animals already having lymphomas. The number of lymphadenomas decreased dependent upon the dosage, as well as the titre of the autoantibodies.

Detailed Description Text (27):
Preparation of a pharmaceutical formulation of imexon

Detailed Description Text (29):
The film tablets were then produced in the usual way by the film drageeing of the imexon cores obtained.

Detailed Description Paragraph Table (1):
TABLE 1

Effect of imexon the proliferation of various cell types BOGF (human B- TGI (MethA) LTT (Splenocytes, ConA) LTT (Splenocytes, PHA) lymphocytes) .sup.3 H-TdR .sup.3 H-TdR .sup.3 H-TdR .sup.3 H-TdR Imexon cpm (n = 6) % inhibi- cpm (n = 6) % inhibi- cpm (n = 6) % inhibi- cpm (n = 6) % inhibi- (.mu.g/ml) - x SD tion - x SD tion - x SD tion - x SD tion

Control 33966 3000 -- 109879 12203 -- 44283 6458 -- 5541 1792 -- (n = 5) 100 534 363 98** 903 62 99** 585 44 99** 562 44 90** 30 911 110 97** 2509 863 98** 573 59 99** 617 59 89** 10 21913 2357 35** 24895 6563 77** 4724 704 89** 574 50 90** 3 35473 3135 -4 118487 9494 -8 35850 13018 19 831 231 85** 1 35475 1753 -4 119120 9172 -8 49348 4168 -11 2096 455 62* 0.3 37593 3080 -11 134032 37682 -22 45542 9870 -3 4201 1636 24 0.1 31722 3991 7 109717 11192 0 41849 1892 5 4847 1146 13

*p < 0.002
**p < 0.001

Detailed Description Paragraph Table (2):
TABLE 2

Results of a comparative investigation of the action of imexon and azidothymidine (AZT) in the Rauscher virus leukaemia model. There are given average values and standard deviations of 5 or 10 fold determinations (Experiment R 17) placebo placebo dose (mg/kg .times. d, i.p.) (-Virus) (+Virus) Imexon 90 Imexon 120 AZT 100 Ribavirin 100 day 7 spleen weight (g) 0.112 .+-. 0.019 (5) 0.091 .+-. 0.045 (10) 0.248 .+-. 0.030 (10) 0.190 .+-. 0.031 (10) 0.185 .+-. 0.017 0.116 .+-. 0.012 (10) animal weight (g) 20.2 .+-. 1.1 (5) 20.7 .+-. 1.3 (10) 21.4 .+-. 1.7 (10) 20.0 .+-. 1.4 (10) 20.0 .+-. 0.8 18.8 .+-. 1.2 (10) day 14 spleen weight (g) 0.165 .+-. 0.013 (5) 0.670 .+-. 0.201 (10) 0.306 .+-. 0.121 (10) 0.238 .+-. 0.076 (10) 0.316 .+-. 0.089 0.260 .+-. 0.060 (7)* animal weight (g) 20.5 .+-. 0.3 (5) 19.6 .+-. 0.9 (10) 19.6 .+-. 1.9 (10) 20.9 .+-. 0.8 (10) 20.9 .+-. 1.1 19.2 .+-. 1.1 (7)* *3 animals died because of toxicity

Detailed Description Paragraph Table (3):
weight/unit/mg.
imexon 100.000 lactose monohydrate 63.000 poly-(0-carboxymethyl)-starch, 7.000 sodium salt poly-(1-vinyl-2-pyrrolidone) 4.000 25,000 poly-(0-carboxymethyl)-starch, 3.000 sodium salt microcrystalline cellulose 20.000 highly dispersed silicon dioxide 1.500 magnesium stearate 1.500 core weight 200.000

CLAIMS:

1. A method of suppressing B-cell proliferation or activation caused by AIDS or ARC, or involved in a B-cell lymphoma or B-cell leukemia, in a patient, said method comprising administering to said patient a B-cell proliferation or activation suppressing amount of Imexon or physiologically acceptable salt thereof.

3. Method of claim 1, wherein the patient is administered about 10 to 1000 mg of Imexon or salt thereof per administration.

4. Method of claim 1, wherein the patient is administered an amount of from 0.1 to 1000 mg/kg of patient body weight of Imexon or salt thereof per administration.

9. Method of claim 1, wherein the Imexon is used as a combination preparation with at least one other anti virally-active substance.

10. Method of claim 1, wherein Imexon or salt thereof is administered to said patient orally, intravenously, subcutaneously or intramuscularly.

12. A method of suppressing B-cell proliferation or activation caused by AIDS or ARC, in a patient, said method comprising administering to said patient a B-cell proliferation or activation suppressing amount of Imexon or physiologically acceptable salt thereof.

13. A method of suppressing B-cell proliferation or activation involved in a B-cell lymphoma or B-cell leukemia, in a patient, said method comprising administering to said patient a B-cell proliferation or activation suppressing amount of Imexon or physiologically acceptable salt thereof.

End of Result Set

L16: Entry 6 of 6 File: USPT Feb 26, 1991

DOCUMENT-IDENTIFIER: US 4996219 A
TITLE: Imidazolidine derivatives as immunosuppressives

Brief Summary Text (39):
For the preparation of pharmaceutical compositions, the compounds according to the present invention are mixed in known manner with appropriate pharmaceutical carrier substances, possibly granulated and pressed, for example into tablets or dragee cores. Filling the mixture into hard capsules is also possible. With the addition of appropriate adjuvant materials, there can also be produced a solution or suspension in water, an oil, such as olive oil, or a high molecular weight polymer, such as polyethylene glycol, and administered as injection solutions, soft gelatine capsules, syrups or drops.

Detailed Description Text (31):
IMEXON=4-imino-1,3-diazabicyclo[3.1.0]hexan-2-one (compound of U.S. Pat. No. 4,083,987)

Detailed Description Paragraph Table (1):
TABLE _____ Test IC.sub.50 (/.mu.g/ml) Compound No. LPT TGI IL 2 BCGF _____ Imexon 6,3 .+-. 1,5 11,3 .+-. 4,4 5,1 .+-. 2,1 0,9 .+-. 0,3 (n = 6) (n = 5) (n = 5) (n = 4) Ex. 1 3,9 .+-. 0.7 >10,3 .+-. 4,1 2,6 .+-. 0,7 1,9 .+-. 1,5 (n = 4) (n = 4) (n = 2) (n = 3) Ex. 2 1 12,0 22,6 >10 .about.4,7 2 11,1 >30 >10 10,6 Ex. 3 1 20,7 >30 >30 >3 2 >10 >10 >10 >10 Ex. 4 1 <3 2,8 <3 <3 2 0,69 1,8 1,2 1,6 3 0,52 3,1 2,0 1,6 Ex. BV11 1 <3 4,2 .ltoreq.3 <3 2 0,92 2,3 3,5 0,71 Ex. BV12 1 <3 7,5 5,1 3,2 2 1,2 3,9 4,6 2,6 3 1,1 4,9 Ex. BV14 1 <3 3,8 <3 <3 2 1,0 2,7 1,3 1,6 3 1,4 5,5 3,6 1,5 Ex. BV16 1 <3 3,9 3,5 <3 2 0,80 5,1 4,8 0,74 3 0,90 5,5 1,1 Ex. BV17 1 <3 <3 <10 <3 2 0,82 2,1 1,4 0,90 3 0,64 3,5 2,4 1,7 _____

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Search Results - Record(s) 1 through 13 of 13 returned.

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1. Document ID: US 6476236 B1

L1: Entry 1 of 13 File: USPT Nov 5, 2002

US-PAT-NO: 6476236
DOCUMENT-IDENTIFIER: US 6476236 B1

TITLE: Synthesis of 2-cyanoaziridine-1-carboxamide

DATE-ISSUED: November 5, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Remers; William	Tuscon	AZ		
Iyengar; Bashyam	Tuscon	AZ		

US-CL-CURRENT: 548/966

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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2. Document ID: US 6331289 B1

L1: Entry 2 of 13 File: USPT Dec 18, 2001

US-PAT-NO: 6331289
DOCUMENT-IDENTIFIER: US 6331289 B1

TITLE: Targeted diagnostic/therapeutic agents having more than one different vectors

DATE-ISSUED: December 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Klaveness; Jo	Olso			NO
Rongved; P.ang.l	Olso			NO
H.o slashed.gset; Anders	Olso			NO
Tolleshaug; Helge	Olso			NO
Cuthbertson; Alan	Olso			NO
Hoff; Lars	Olso			NO
Bryn; Klaus	Olso			NO
Hellebust; Halldis	Olso			NO
Solbakken; Magne	Olso			NO

US-CL-CURRENT: 424/9.52; 424/1.21, 424/450, 424/9.4, 424/9.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 3. Document ID: US 6297230 B1

L1: Entry 3 of 13 File: USPT Oct 2, 2001

US-PAT-NO: 6297230
DOCUMENT-IDENTIFIER: US 6297230 B1

TITLE: Cyanoaziridines for treating cancer

DATE-ISSUED: October 2, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Remers; William A.	Tucson	AZ		
Hersh; Evan M.	Tucson	AZ		
Dorr; Robert T.	Tucson	AZ		
Iyengar; Bhashyam	Tucson	AZ		

US-CL-CURRENT: 514/183; 548/966, 548/967, 558/434

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 4. Document ID: US 6264917 B1

L1: Entry 4 of 13 File: USPT Jul 24, 2001

US-PAT-NO: 6264917
DOCUMENT-IDENTIFIER: US 6264917 B1

TITLE: Targeted ultrasound contrast agents

DATE-ISSUED: July 24, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Klaveness; Jo	Oslo			NO
Rongved; P.ang.l	Oslo			NO
L.o slashed.vhaug; Dagfinn	Oslo			NO

US-CL-CURRENT: 424/9.52; 600/458

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 5. Document ID: US 6261537 B1

L1: Entry 5 of 13 File: USPT Jul 17, 2001

US-PAT-NO: 6261537
DOCUMENT-IDENTIFIER: US 6261537 B1

TITLE: Diagnostic/therapeutic agents having microbubbles coupled to one or more vectors

DATE-ISSUED: July 17, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Klaveness; Jo	Oslo			NO
Rongved; P.ang.l	Oslo			NO
H.o slashed.gset; Anders	Oslo			NO
Tolleshaug; Helge	Oslo			NO
N.ae butted.vestad; Anne	Oslo			NO
Hellebust; Halldis	Oslo			NO
Hoff; Lars	Oslo			NO
Cuthbertson; Alan	Oslo			NO
L.o slashed.vhaug; Dagfinn	Oslo			NO
Solbakken; Magne	Oslo			NO

US-CL-CURRENT: 424/9.52; 424/1.29, 424/489, 424/9.32, 424/9.4, 424/9.6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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6. Document ID: US 5369119 A

L1: Entry 6 of 13 File: USPT Nov 29, 1994

US-PAT-NO: 5369119
DOCUMENT-IDENTIFIER: US 5369119 A

TITLE: Use of imexon as an immune suppressive and pharmaceutical compositions containing imexon

DATE-ISSUED: November 29, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Herrmann; Dieter	Heidelberg			DE
Haag; Rainer	Ladenburg			DE
Bosies; Elmar	Weinheim			DE
Bicker; Uwe	Bensheim			DE
Kampe; Wolfgang	Heddesheim			DE

US-CL-CURRENT: 514/389; 514/50, 514/885

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 7. Document ID: US 4996219 A

L1: Entry 7 of 13 File: USPT Feb 26, 1991

US-PAT-NO: 4996219
DOCUMENT-IDENTIFIER: US 4996219 A

TITLE: Imidazolidine derivatives as immunosuppressives

DATE-ISSUED: February 26, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsaklakidis; Christos	Weinheim			DE
Bosies; Elmar	Weinheim			DE
Schultz; Michael	Mannheim			DE
Haag; Rainer	Ladenburg			DE
Herrmann; Dieter	Heidelberg			DE
Pahlke; Wulf	Bensheim			DE

US-CL-CURRENT: 514/341; 514/333, 514/389, 546/256, 546/274.4, 546/274.7, 548/315.1, 548/315.4, 548/315.7, 548/321.5, 548/331.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | PDMC | Draw Desc | Image

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☐ 8. Document ID: JP 02088521 A

L1: Entry 8 of 13 File: JPAB Mar 28, 1990

PUB-NO: JP402088521A
DOCUMENT-IDENTIFIER: JP 02088521 A
TITLE: PHARMACEUTICAL AGENT HAVING IMMUNOSUPPRESSIVE ACTION

PUBN-DATE: March 28, 1990

INVENTOR-INFORMATION:

NAME	COUNTRY
HERRMANN, DIETER	
HAAG, RAINER	
BOSIES, ELMAR	
BICKER, UWE	
KAMPE, WOLFGANG	

INT-CL (IPC): A61K 31/395; A61K 31/395

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | PDMC | Draw Desc | Image

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☐ 9. Document ID: DE 3844839 A1

L1: Entry 9 of 13 File: EPAB Apr 30, 1992

PUB-NO: DE003844839A1
DOCUMENT-IDENTIFIER: DE 3844839 A1
TITLE: TITLE DATA NOT AVAILABLE

PUBN-DATE: April 30, 1992

INT-CL (IPC): A61K 31/415

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | Draw Desc | Image

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☐ 10. Document ID: DE 3844655 A1

L1: Entry 10 of 13 File: EPAB May 17, 1990

PUB-NO: DE003844655A1
DOCUMENT-IDENTIFIER: DE 3844655 A1
TITLE: Use of imexon as immunosuppressant

PUBN-DATE: May 17, 1990

INVENTOR-INFORMATION:

NAME	COUNTRY
BICKER, UWE PROF	DE
BOSIES, ELMAR DR PHIL	DE
HAAG, RAINER DIPL CHEM DR RER N	DE
HERRMANN, DIETER DR MED	DE
KAMPE, WOLFGANG DR RER NAT	DE

INT-CL (IPC): A61K 31/495; A61K 31/70
EUR-CL (EPC): A61K031/415; A61K031/70

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | Draw Desc | Image

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☐ 11. Document ID: EP 352652 A2

L1: Entry 11 of 13 File: EPAB Jan 31, 1990

PUB-NO: EP000352652A2
DOCUMENT-IDENTIFIER: EP 352652 A2
TITLE: Use of imexone as an immunosuppressive agent.

PUBN-DATE: January 31, 1990

INVENTOR-INFORMATION:

NAME	COUNTRY
HERRMANN, DIETER DR MED	
HAAG, RAINER DR RER NAT	
BOSIES, ELMAR DR PHIL NAT	
BICKER, UWE PROF DR	
KAMPE, WOLFGANG DR RER NAT	

INT-CL (IPC): A61K 31/395; A61K 31/415; A61K 31/505
EUR-CL (EPC): A61K031/505

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | PwwC | Draw Desc | Image

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☐ 12. Document ID: AU 200216672 A WO 200241871 A2

L1: Entry 12 of 13 File: DWPI Jun 3, 2002

DERWENT-ACC-NO: 2002-471692
DERWENT-WEEK: 200263
COPYRIGHT 2003 DERWENT INFORMATION LTD
TITLE: Liposomal composition useful for the treatment of cancer comprises imexon or its derivative and at least one lipid

INVENTOR: HERSH, E M; LOPEZ-BERESTEIN, G ; REMERS, W A

PRIORITY-DATA: 2000US-0721040 (November 21, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 200216672 A	June 3, 2002		000	A61K009/00
WO 200241871 A2	May 30, 2002	E	107	A61K009/00

INT-CL (IPC): A61 K 9/00

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | PwwC | Draw Desc | Image

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☐ 13. Document ID: EP 352652 A PT 91293 A AU 8938877 A DE 3825667 A DK 8903633 A JP 02088521 A DE 3844655 A ZA 8905710 A HU 52378 T DE 3825667 C DE 3844839 A DE 3844655 C HU 206827 B DE 3844839 C2 IL 91138 A US 5369119 A EP 352652 B1 CA 1333771 C DE 58908926 G IE 66680 B PH 26684 A JP 2848634 B2 KR 135757 B1

L1: Entry 13 of 13 File: DWPI Jan 31, 1990

DERWENT-ACC-NO: 1990-031242
DERWENT-WEEK: 200151
COPYRIGHT 2003 DERWENT INFORMATION LTD
TITLE: Use of imexon as immunosuppressant acting selectively on B cells - for treating and preventing e.g. auto:immune diseases and viral infections, partic. AIDS

INVENTOR: BICKER, U; BOSIES, E ; HAAG, R ; HERRMANN, D ; KAMPE, W ; HERMANN, D ; KAMPE, ; HERREMANN, D ; BOEHRINGER MANNHEIM GMBH,

PRIORITY-DATA: 1988DE-3825667 (July 28, 1988), 1988DE-3844655 (July 28, 1988), 1988DE-0844655 (), 1988DE-3844839 (July 28, 1988)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 352652 A	January 31, 1990	G	009	
PT 91293 A	February 8, 1990		000	
AU 8938877 A	February 1, 1990		000	
DE 3825667 A	March 15, 1990		000	
DK 8903633 A	January 29, 1990		000	
JP 02088521 A	March 28, 1990		000	
DE 3844655 A	May 17, 1990		000	
ZA 8905710 A	April 25, 1990		000	
HU 52378 T	July 30, 1990		000	
DE 3825667 C	June 27, 1991		000	
DE 3844839 A	April 30, 1992		000	
DE 3844655 C	July 30, 1992		006	A61K031/415
HU 206827 B	January 28, 1993		000	A61K031/415
DE 3844839 C2	June 9, 1994		006	A61K031/415
IL 91138 A	October 21, 1994		000	A61K031/415
US 5369119 A	November 29, 1994		005	A61K031/415
EP 352652 B1	January 25, 1995	G	009	A61K031/415
CA 1333771 C	January 3, 1995		000	A61K031/505
DE 58908926 G	March 9, 1995		000	A61K031/415
IE 66680 B	January 24, 1996		000	A61K031/415
PH 26684 A	September 15, 1992		000	A61K031/415
JP 2848634 B2	January 20, 1999		007	A61K031/395
KR 135757 B1	April 23, 1998		000	A61K031/415

INT-CL (IPC): A61K 9/20; A61K 31/395; A61K 31/41; A61K 31/415; A61K 31/50; A61K 31/505; C07D 487/04; C07K 7/64; G01N 33/50

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Terms	Documents
imexon	13

Display Format: Change Format

Previous Page Next Page

WEST Search History

DATE: Wednesday, November 12, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L2	L1 and (liposome$ or lipid$)	4	L2
L1	imexon	13	L1

END OF SEARCH HISTORY

Title compds. (I; R1-R3 = H, alkyl; R4 = cyano, carboxamide, carboxylate ester) were prepd. by reaction of the corresponding unacylated aziridines with R5NCO (R5 = COR6; R6 = haloalkyl) followed by treatment of the intermediate with a nucleophile. In addn., the invention provides a process for producing 4-imino-1,3-diazabicyclo[3.1.0]-hexan-2-ones (II; variables as above) from I. Thus, 2-cyanoaziridine in PhMe was added over 1 h to Cl3CCONCO in PhMe at -10.degre . followed by stirring for addnl. 1 h storage overnight at 5.degree. to give 2-cyanoaziridine-1-[N-(trichloroacetyl)]carboxamide. The latter was stirred with NH3 in MeOH at 0.degree. for 1.5 h to give 2-cyanoaziridine-2-carboxamide.

.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2003 ACS
2002:408506 CAPLUS
137:10970
Liposomal compositions comprising **imexon** derivatives
Lopez-Berestein, Gabriel; Remers, William A.; Hersh, Evan M.
Board of Regents, the University of Texas System, USA; Arizona Board of Regents, University of Arizona
PCT Int. Appl., 106 pp.
CODEN: PIXXD2
Patent
English

N.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002041871	A2	20020530	WO 2001-US43292	20011120
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2002016672	A5	20020603	AU 2002-16672	20011120
AI US 2000-721040	A1	20001121		
WO 2001-US43292	W	20011120		

Disclosed are novel compns. comprising a lipid and **imexon** or a deriv. thereof. Also disclosed are liposomal compns. comprising **imexon** or deriv. thereof. Methods for administering pharmaceutically acceptable compns. comprising a lipid and **imexon** or a deriv. thereof for the treatment of diseases, such as cancer, are also disclosed herein. Thus, 2-cyanoaziridine-1-(N-methyl)carboxamide (I) was prepd. by the reaction of 2-cyanoaziridine with Me isocyanate. Antitumor activity of liposomal I was tested against a panel of tumor cells in culture.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2003 ACS
2002:95271 CAPLUS
136:395484
Molecular and cellular characterization of **imexon**-resistant RPMI8226/I myeloma cells
Dvorakova, Katerina; Payne, Claire M.; Tome, Margaret E.; Briehl, Margaret M.; Vasquez, Miguel A.; Waltmire, Caroline N.; Coon, Amy; Dorr, Robert T.
Arizona Cancer Center, University of Arizona, Tucson, AZ, 85724, USA
Molecular Cancer Therapeutics (2002), 1(3), 185-195
CODEN: MCTOCF; ISSN: 1535-7163
American Association for Cancer Research
Journal
English
Imexon is an aziridine-contg. iminopyrrolidone with selective growth-inhibitory potency for multiple myeloma. Our previous research indicates that **imexon** induces mitochondrial alterations, oxidative stress, and apoptosis. This drug represents an interesting model drug with a nonmyelosuppressive profile to study the basic mechanisms leading to antitumor activity and resistance. The major

purpose of this study was to characterize an **imex** n-resistant RPMI8226/I cell line that was developed from RPMI8226 cells by continuous exposure to **imexon**. No significant differences were obsd. in the sensitivity to several cytotoxic drugs, including mitoxantrone, mitomycin C, melphalan, methotrexate, cytarabine, cisplatin, vincristine, and paclitaxel, in the **imexon**-resistant cells. How ver, RPMI8226/I cells were cross-resistant to arsenic trioxide, doxorubicin, fluorouracil, etoposide, irinotecan, and esp. IFN-.alpha.. The data from DNA microarray and Western blot analyses indicated that the levels of antiapoptotic proteins Bcl-2 and thioredoxin-2, which reside mainly in the mitochondria, are increased in RPMI8226/I cells. In addn., increased levels of lung resistance protein were detected in **imexon** -resistant cells. Expression of P-glycoprotein was not detected in RPMI8226/I cells. No loss of mitochondrial membrane potential or increase in the levels of reactive oxygen species was obsd. in RPMI8226/I cells after exposure to **imexon**; however, the levels of glutathione are increased in the RPMI8226/I cells. TEM revealed significant changes in the mitochondrial morphol. of RPMI8226/I cells, whereas no ultrastructural changes were obsd. in other cellular compartments. **Imexon** -resistant RPMI8226/I myeloma cells appear to have a unique mechanism of resistance that is assocd. with morphol. alterations of mitochondria, increased protection against oxidative stress, elevated levels of glutathione, and enhanced expression of antiapoptotic mitochondrial proteins.

.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2003 ACS
2001:417780 CAPLUS
135:220890
Induction of mitochondrial changes in myeloma cells by **imexon**
Dvorakova, Katerina; Waltmire, Caroline N.; Payne, Claire M.; Tome, Margaret E.; Briehl, Margaret M.; Dorr, Robert T.
Arizona Cancer Center, Department of Microbiology and Immunology, University of Arizona, Tucson, AZ, USA
Blood (2001), 97(11), 3544-3551
CODEN: BLOOAW; ISSN: 0006-4971
American Society of Hematology
Journal
English

Imexon is a cyanoaziridine deriv. that has antitumor activity in multiple myeloma. Previous studies have shown that **imexon** induces oxidative stress and apoptosis in the RPMI 8226 myeloma cell line. This study reports that **imexon** has cytotoxic activity in other malignant cell lines including NCI-H929 myeloma cells and NB-4 acute promyelocytic leukemia cells, whereas normal lymphocytes and U266 myeloma cells are substantially less sensitive. Flow cytometric expts. have shown that **imexon** treatment is assocd. with the formation of reactive oxygen species (ROS) and the loss of mitochondrial membrane potential (.DELTA..psi.m) in **imexon**-sensitive myeloma cell lines and NB-4 cells. In contrast, redn. of .DELTA..psi.m and increased levels of ROS were not obsd. in **imexon**-resistant U266 cells. Treatment of **imexon**-sensitive RPMI 8226 cells with the antioxidant N-acetyl-L-cysteine (NAC) protects cells against these effects of **imexon**. Mitochondrial swelling was obsd. by electron microscopy in RPMI 8226 myeloma cells treated with 180 .mu.M **imexon** as early as 4 h. Damage to mitochondrial DNA was detected by a semiquant. polymerase chain reaction assay in **imexon**-treated RPMI 8226 c lls; however, nuclear DNA was not affected. Finally, partial protection of RPMI 8226 cells against the **imexon** effects was achieved by treatment with thenoyltrifluoroacetone, an inhibitor of superoxide prodn. at mitochondrial complex II. These changes are consistent with mitochondrial oxidn. and apoptotic signaling as mediators of the growth inhibitory effects of **imexon**. Interestingly, oxidative damage and decrease of .DELTA..psi.m induced by **imexon** highly correlates with sensitivity to **im xon** in several myeloma cell lines and an acute promyelocytic leukemia cell line.

CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2003 ACS
2001:264704 CAPLUS
135:40605
Mechanisms of **imexon** action in human myeloma cells
Dvorakova, Katerina
Univ. of Arizona, Tucson, AZ, USA
(2000) 151 pp. Avail.: UMI, Order No. DA9972072
From: Diss. Abstr. Int., B 2000, 61(5), 2484
Dissertation
English
Unavailable

ANSWER 7 OF 22 CAPLUS COPYRIGHT 2003 ACS
2000:531351 CAPLUS
133:246877
Induction of oxidative stress and apoptosis in myeloma cells by the aziridine-containing agent **imexon**
Dvorakova, K.; Payne, C. M.; Tome, M. E.; Briehl, M. M.; McClure, T.; Dorr, R. T.
Arizona Cancer Center, The University of Arizona, Tucson, AZ, 85724, USA
Biochemical Pharmacology (2000), 60(6), 749-758
CODEN: BCPCA6; ISSN: 0006-2952
Elsevier Science Inc.
Journal
English
Imexon is an iminopyrrolidone deriv. that has selective antitumor activity in multiple myeloma. The exact mechanism of **imexon** action is unknown. In human 8226 myeloma cells, the cytotoxicity of **imexon** was schedule-dependent, and long exposures (.gtoreq.48 h) to low concns. of **imexon** were most effective at inducing cytotoxicity. Our data suggest that **imexon** does not affect DNA, but it can alkylate thiols by binding to the sulfhydryl group. We have also demonstrated by HPLC studies that in human 8226 myeloma cells, **imexon** depletes cellular stores of cysteine and glutathione. Oxidative stress in 8226 cells exposed to **imexon** was detected by immunohistochem. staining with a monoclonal antibody to 8-hydroxydeoxyguanosine (8-OHdG), followed by confocal microscopy. These images showed increased levels of 8-OHdG in the cytoplasm of cells treated with different concns. of **imexon** at 8, 16, and 48 h. Interestingly, 8-OHdG staining was not obsd. in the nuclei of **imexon**-treated cells, in contrast to the diffuse staining seen with t-Bu hydroperoxide. Myeloma cells exposed to **imexon** showed classic morphol. features of apoptosis upon electron microscopy, and increased levels of phosphatidylserine exposure, detected as Annexin-V binding, on the cell surface. To prevent depletion of thiols, 8226 myeloma cells exposed to **imexon** were treated with N-acetylcysteine (NAC). Simultaneous, as well as sequential, treatment with NAC before **imexon** exposure resulted in protection of myeloma cells against **imexon**-induced cytotoxicity. Conversely, the glutathione synthesis inhibitor buthionine sulfoximine increased **imex n** cytotoxicity. These data suggest that **imexon** perturbs cellular thiols and induces oxidative stress leading to apoptosis in human myeloma cells.
CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2003 ACS
1999:401696 CAPLUS
131:43589
Diagnostics and therapeutics for transmissible spongiform encephalopathy and methods for the manufacture of non-infective blood products and tissue derived products
Aguzzi, Adriano; Klein, Michael A.; Raeber, Alex; Weissmann, Charles; Zinkernagel, Rolf
University of Zurich, Switz.
PCT Int. Appl., 162 pp.
CODEN: PIXXD2
Patent

English
N.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930738	A2	19990624	WO 1998-EP8271	19981216
WO 9930738	A3	19991021		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 931551	A1	19990728	EP 1997-122186	19971216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1214943	A1	20020619	EP 2001-127424	19971216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1215497	A1	20020619	EP 2001-127425	19971216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AU 9926131	A1	19990705	AU 1999-26131	19981216
EP 1044020	A2	20001018	EP 1998-966899	19981216
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2002508335	T2	20020319	JP 2000-538717	19981216

AI EP 1997-122186 A 19971216
WO 1998-EP8271 W 19981216

B-cells have been identified as being the crucial carriers of infectivity in the spread of transmissible spongiform encephalopathy within an infected organism. In a second step, B-cells may infect further components of the immune system, e.g. T-cells. Accordingly, the present invention provides B-cell and T-cell specific ligands for the use in diagnostics and therapeutics for transmissible spongiform encephalopathy and provides methods for the manuf. of non-infective blood products and tissue derived products. Thus, the present invention provides medicaments comprising B-cell and/or T-cell depletants, for the treatment of pathologies where the depletion of B-cells and/or T-cells, and more particularly of tse-infected B-cells and/or T-cells is therapeutically effective. The B cell depletant includes anti-B cell antibody such as rituximab and B220 or chem. compd. such as **imexon** and ciamexone; the T cell depletant includes anti-T cell antibody or chem. compd. such as cyclosporin A; and B/T cell depletant includes combination of cyclophosphamide and dexamethasone.

ANSWER 9 OF 22 CAPLUS COPYRIGHT 2003 ACS
1999:59396 CAPLUS
130:261455
Novel Antitumor 2-Cyanoaziridine-1-carboxamides
Iyengar, Bhashyam S.; Dorr, Robert T.; Alberts, David S.; Hersh, Evan M.; Salmon, Sydney E.; Remers, William A.
Department of Pharmacology and Toxicology and Arizona Cancer Center, University of Arizona, Tucson, AZ, 85721, USA
Journal of Medicinal Chemistry (1999), 42(3), 510-514
CODEN: JMCMAR; ISSN: 0022-2623
American Chemical Society
Journal
English

A set of 20 2-cyanoaziridine-1-carboxamides was synth sized from 2-cyanoaziridine and appropriate isocyanates. These compds. were active against a variety of solid and hematol. tumor cells in culture, including strains resistant to doxorubicin and mitoxantrone. Their potencies in these assays correlated with the lipophilicity of substituents. The N-Ph deriv. was more potent and equally effective to **im xon**, a cyclized 2-cyanoaziridine-1-carboxamide of clin. interest, against cloned fresh human tumors.

CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 22 CAPLUS COPYRIGHT 2003 ACS
1996:68824 CAPLUS
124:135035
Preclinical pharmacokinetics and antitumor activity of **imexon**
Dorr, Robert T.; Liddil, James D.; Klein, Mary Kay; Hersh, Evan M.
Arizona Cancer Center, College Medicine, Tucson, AZ, 85724, USA
Investigational New Drugs (1995), 13(2), 113-16
CODEN: INNDDK; ISSN: 0167-6997
Kluwer
Journal
English
Im xon is an aziridine compd. originally studied for immune-enhancing effects on lymphocytes. The drug was well-tolerated in humans and was shown to be active in a variety of animal tumor models. Recently, **imexon** has demonstrated antitumor activity in human multiple myeloma cell lines in vitro. The pharmacokinetics of the compd. using a normal phase HPLC assay were studied in normal mice and in dogs with mast cell tumors. Doses of 100 mg/kg given i.p. produced peak plasma levels over 100 .mu.g/mL in mice and the drug was rapidly eliminated with half lives of 8 min (.alpha. phase) and 29 min (.beta. phase). Only 20% of an oral **imexon** dose was absorbed in the mouse. In dogs, the .alpha. and .beta. phase half lives ranged from 18-26 min and 91-110 min, resp. Peak levels over 100 .mu.g/mL were obtained following i.v. doses of 12.5 mg/kg and 25 mg/kg. **Imexon** was active in mice bearing either P-388 or L-1210 leukemia, but not in mice with B-16 melanoma. These results suggest that cytotoxic drug concns. can be obtained in vivo and that **imexon** is active in lymphoproliferative tumors.

ANSWER 11 OF 22 CAPLUS COPYRIGHT 2003 ACS
1994:692072 CAPLUS
121:292072
Antiviral and immunomodulating inhibitors of experimentally-induced Punta Toro virus infections
Sidwell, Robert W.; Huffman, John H.; Barnard, Dale L.; Smee, Donald F.; Warren, Reed P.; Chirigos, Michael A.; Kende, Meir; Huggins, John
Institute for Antiviral Research, Utah State University, Logan, UT, 84322-5600, USA
Antiviral Research (1994), 25(2), 105-22
CODEN: ARSRDR; ISSN: 0166-3542
Elsevier
Journal
English
A major component of a US Army Medical Research and Development Command-supported program to discover and develop new drugs for the treatment of Rift Valley fever, sandfly fever, and Crimean-Congo hemorrhagic fever has been to study candidate test materials against hepatotropic infections of C57BL/6 mice induced by the related but less biohazardous Punta Toro virus (PTV). The effects of 75 compds., some of which were considered immunomodulators in their primary mechanism of activity, were studied in the PTV infection model. Of these, ribavirin, ribamidine, ribavirin 2',3',5'-triacetate, tiazofurin, tiazofurin-5'-monophosphate, tiazofurin-2',3',5'-triacetate, selenazofurin, pyrazofurin, 3-deazaguanine, and 3-deazaguanosine were considered significantly inhibitory, acting against the infection by a direct antiviral (non-immunomodulatory) fashion. These compds. had therapeutic indexes (TI) ranging from .gtoreq.5 to 65, using increased survivors as the evaluation parameter. Immunomodulators considered significantly inhibitory to this infection were poly (ICLC), ampligen, human recombinant interferon-.alpha.-A/D, MVE-1, MVE-2, AM-3, AM-5, mannozym, bropirimine, CL246,738, phenyleneamine, and 7-thia-8-oxoguanosine. Utilizing increased survivor nos. as measure of activity, these inhibitors had TI ranging from .gtoreq.16 to 1000. Other antiviral effects exerted by the active compds. included redn. of hepatic icterus, lowered serum glutamic oxaloacetic and pyruvic acid transaminases, and inhibition of recoverable serum and liver virus titers. The active immunomodulators were significantly effective when therapy was initiated as late as 48 h after virus inoculation, at a time when clin. signs of the PTV disease were being manifested in the animal.

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2003 ACS
1993:573802 CAPLUS
119:173802
Immunomodulator effects on the Friend virus infection in genetically defined mice
Sidwell, R. W.; Morrey, J. D.; Okleberry, K. M.; Burger, R. A.; Warren, R. P.
Inst. Antiviral Res., Utah State Univ., Logan, UT, 84322-5600, USA
Annals of the New York Academy of Sciences (1993), 685(Immunomodulating Drugs), 432-46
CODEN: ANYAA9; ISSN: 0077-8923
Journal
English
The disease induced by the Friend virus complex (FV) in F1 hybrid mice contg. the Rff-3r/s genotype in the presence of H-2a/a was used to evaluate a variety of immunomodulating substances. In these genetically defined mice, the FV disease results in splenomegaly, early prodn. of high titers of cell-assocd. and plasma virus, high; levels of splenic viral RNA, increased hematocrit, and eventual death. As the disease progresses, reduced levels of infectious virus correlate with development of specific antibody; redn. in T cell populations, increase in B cells, and decrease in T-cell function also occur. The following immunomodulators were evaluated, listed in the order of their ability to inhibit the FV disease: **imexon** > MVE-2 > human recombinant IFN-a A/D > AS101 > ampligen > AM-3 = > ImuVert > bropirimine. In fact, bropirimine, used with certain treatment regimens, appeared to enhance the FV disease. These data suggest that certain immunomodulators may have potential value in the treatment of HIV disease, but also indicate that caution should by exercised in their clin. use.

ANSWER 13 OF 22 CAPLUS COPYRIGHT 2003 ACS
1992:584412 CAPLUS
117:184412
Antiproliferative and antitumor activity of the 2-cyanoaziridine compound **imexon** on tumor cell lines and fresh tumor cells in vitro
Hersh, Evan M.; Gschwind, Charles R.; Taylor, Charles W.; Dorr, Robert T.; Taetle, Raymond; Salmon, Sydney E.
Sect. Hematol. Oncol., Arizona Cancer Cent., Tucson, AZ, 85724, USA
Journal of the National Cancer Institute (1992), 84(16), 1238-44
CODEN: JNCIEQ; ISSN: 0027-8874
Journal
English
The concn. of **imexon** that caused 50% inhibition of cell growth was <10 .mu.g/mL for mitogen-stimulated lymphocytes and was 3-10 .mu.g/mL for B-cell lymphomas and both multidrug-resistant and -sensitive myeloma cell lines. **Imexon** inhibited 4 of 7 fresh lymphoma and 11 of 16 fresh myeloma biopsy specimens to <40% of control growth. A 1-h exposure of lymphoma cells to 50-100 .mu.g **imexon**/mL, followed by removal of drug and continuing culture, resulted in >95% inhibition during the next 48-72 h. **Imexon** selectively inhibited protein formation during the 1st 24-48 h of exposure of lymphoma and myeloma cells. Cells exposed to inhibitory concns. of **imexon** were blocked in cell cycle progression. **Imexon** may be a useful agent in the treatment of malignant diseases, exp. lymphoid malignancies.

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2003 ACS
1992:524079 CAPLUS
117:124079
Treatment of the murine, retrovirus-induced lymphoproliferative immunodeficiency disease (LP-BM5) in C57BL/10 mice with the immunomodulator **imexon**
Funk, Carole Y.; Eisman, Julia; Hersh, Evan M.
Sect. Hematol. Oncol., Arizona Cancer Cent., Tucson, AZ, 85724, USA
AIDS Research and Human Retroviruses (1992), 8(5), 633-8
CODEN: ARHRE7; ISSN: 0889-2229
Journal
English
Imexon (4-imino-1,3-diazabicyclo-(3.1.0)-hexan-2-one) a

cyanoaziridine compd. was studied in the treatment of the murine retrovirus-induced immunodeficiency disease model of AIDS (LP-BM5, MAIDS). **Imexon**, in dose-dependent fashion, partially prevented the development of hypergammaglobulinemia and splenomegaly, and partially prevented the decline in the phytohemagglutinin-induced proliferative response of spleen lymphocytes when started 1 or 15 days after virus inoculation. There was a statistically significant redn. in these dis ase-assocd. manifestations. When animals were treated starting 78 or 92 days after virus inoculation, lymphadenopathy was completely abrogated and survival was significantly prolonged in a dose-responsive manner. Since **imexon** and other cyanoaziridine compds. have been safely administered to humans, the authors suggest that this class of compds. be further investigated in both large animal models of HIV infection and in patients with HIV-induced disease.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2003 ACS
1992:247956 CAPLUS
116:247956
Imexon and biological response modifiers in murine models of AIDS
Chirigos, Michael A.; Ussery, Michael A.; Black, Paul L.
U. S. Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21702, USA
International Journal of Immunopharmacology (1991), 13(Suppl. 1), 33-41
CODEN: IJIMDS; ISSN: 0192-0561
Journal
English
The Rauscher murine leukemia retrovirus system provides an in vivo model of th human acquired immune deficiency syndrome for testing the ability of antiviral agents and biol. response modifiers (BRM) to suppress viremia and retroviral disease. In the present report the authors examd. three agents in the Rauscher retrovirus model: **imexon**, Ampligen and poly[I,C]-LC. **Imexon** reduced splenomegaly, viremia, and serum reverse transcriptase levels even when treatment was not initiated until 7 days after virus infection. **Imexon** also significantly prolonged the survival of infected mice. Thus it proved to be an effective antiviral agent in this system, although **imexon** did not completely eliminate retroviral infection in treated mice. Poly[I,C]-LC and Ampligen had immunomodulatory effects. Both of these BRM augmented the cytolytic activity of splenic natural killer (NK) cells in infected animals when treatment was initiated 24 h after infection. Poly[I,C]-LC had antiretroviral activity when administered on this schedule. In order to examine the role of NK cell augmentation in the antiviral activity of poly[I,C]-LC, the authors attempted to deplete NK activity by treatment with rabbit antibody to asialo-GM1, a ganglioside on the surface of murine NK cells. Combined treatment of infected mice with poly[I,C]-LC and anti-asialo-GM1 decreased the antiviral activity of poly[I,C]-LC. This finding suggests that NK cells may be involved in the antiviral effect of this BRM.

ANSWER 16 OF 22 CAPLUS COPYRIGHT 2003 ACS
1992:187557 CAPLUS
116:187557
Elucidation of mode of retroviral-inhibitory effects of **imexon** through use of immune competent and severe combined immune deficiency (SCID) mice
Morrey, John D.; Mead, Jan R.; Warren, Reed P.; Okleberry, Kevin M.; Burger, Roger A.; Sidwell, Robert W.
AIDS Res. Program, Utah State Univ., Logan, UT, 84322-5600, USA
Antiviral Research (1992), 17(3), 223-33
CODEN: ARSRDR; ISSN: 0166-3542
Journal
English
Mice infected with various tumor retroviruses have been used as models for evaluating therapeutic substances for the treatment of some cancers, and more recently, for human immunodeficiency virus (HIV) infection, the causative agent of acquired immune deficiency syndrome (AIDS). Consequently, there is a need to det. the ability of biol. response modifiers (BRMs) to specifically reduce virus-infected cells, as compared to their non-specific antiproliferative effects. To address this need, a

BRM, **imexon**, was evaluated in this study using three strains of mice having different Friend virus (FV)-specific immunol. capabilities. The first strain, (B10.A .times. A/WySn)F1, was genetically capable of producing FV-specific neutralization and cytotoxic antibodies, the second, Balb/c, was not, and the third, SCID mice, lacked functional T and B cell immunity. **Imexon** treatment reduced virally-induced splenomegaly in all 3 strains; however, the concn. of splenic viral infectious centers (IC) were not affected. Since **imexon** was efficacious in reducing splenomegaly in SCID mice, the mode of action was concluded to not require functional T or B cell immunity. The observation that **imexon** did not affect splenic IC titers also suggested that **imex n** did not specifically eliminate virally infected cells, but may have functioned by other mechanisms. This study also demonstrated the use of various mouse strains as a strategy for delineating the modes of action of BRMs against murine retroviral infections.

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2003 ACS
1991:220817 CAPLUS
114:220817
Effect of **imexon** treatment on Friend virus complex infection using genetically defined mice as a model for HIV-1 infection
Morrey, John D.; Warren, Reed P.; Okleberry, Kevin M.; Burger, Roger A.; Chirigos, Michael A.; Sidwell, Robert W.
AIDS Res. Program, Utah State Univ., Logan, UT, 84322-5600, USA
Antiviral Research (1991), 15(1), 51-65
CODEN: ARSRDR; ISSN: 0166-3542
Journal
English
Imex n was moderately effective in the treatment of a retroviral infection in a genetically defined murine model. The animal model consisted of a Friend virus complex (FV) infection in a hybrid mouse strain, (B 10.A .times. A/WySn)F1 which has similarities with acquired immune deficiency syndrome (AIDS). I.p. **imexon**, initiated 1 or 3 days after FV inoculation and continued through 13 days after inoculation, reduced splenomegaly, splenic cell-free virus titers and viral RNA. Viral infectious centers/106 splenocytes and FV titers in the plasma were reduced, though not significantly. The effect of **imex n** on survival was not significant, which suggested that the antiviral effects were only transiently. Phytohemagglutinin-induced blastogenesis and the percentage of total T cells, T helper cells and T suppressor/cytotoxic cells in the spleens were increased, and the percentage of B cells decreased, by **imexon** treatment of both FV-infected and uninfected mice. Splenic natural killer cell activity and interleukin-1 prodn. were not markedly affected. Virus-specific neutralizing antibody developed in both **imexon**- and placebo-treated FV-infected mice, although titers were lower in the **imexon**-treated animals.

ANSWER 18 OF 22 CAPLUS COPYRIGHT 2003 ACS
1990:490967 CAPLUS
113:90967
Antiviral efficacy of **imexon** in the Rauscher murine retrovirus AIDS model
Chirigos, Michael A.; Ussery, Michael A.; Rankin, James T., Jr.; Herrmann, Dieter; Bicker, Uwe; Black, Paul L.
South Res. Inst., U. S. Army Med. Res. Inst. Infect. Dis., Ft. Detrick, MD, 21701, USA
Immunopharmacology and Immunotoxicology (1990), 12(1), 1-21
CODEN: IITOEF; ISSN: 0892-3973
Journal
English
The antiviral effects of **imexon** (I) were studied in BALB/c mice at different stages of infection with erythrotropic Ranscher murine leukemia virus (RMLV). AZT and ribavirin were used as pos. internal controls. The treatment with I (90 and 120 mg/kg) led to a suppression of splenomegaly by .gtoreq.50% as well as a decrease in viremia and serum reverse transcriptase (RT) levels. No differences were noted whether therapy was initiated one day prior to or on the same day of the RMLV inoculation. The drug was very effective in suppressing splenomegaly,

viremia, and RT when mice were sacrificed 14 days following treatment. However, there was a progressive decrease in body wt. assocd. with the higher concns. of I (10 and 18% decrease at the 170 and 220 mg/kg of I, resp.). Continuous treatment with 110 and 170 mg/kg for 20 days showed that I maintained its therapeutic effectiveness.

ANSWER 19 OF 22 CAPLUS COPYRIGHT 2003 ACS
1990:191949 CAPLUS
112:191949
Use of **imexon** as an immunosuppressive agent
Herrmann, Dieter; Haag, Rainer; Bosies, Elmar; Bicker, Uwe; Kampe, Wolfgang
Boehringer Mannheim G.m.b.H., Germany
Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
Pat nt
German
J.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 352652	A2	19900131	EP 1989-113425	19890721
EP 352652	A3	19910904		
EP 352652	B1	19950125		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 3825667	A1	19900315	DE 1988-3825667	19880728
DE 3825667	C2	19910627		
DE 3844655	A1	19900517	DE 1988-3844655	19880728
DE 3844655	C2	19920730		
DE 3844839	C2	19940609	DE 1988-3844839	19880728
DK 8903633	A	19900129	DK 1989-3633	19890721
AU 8938877	A1	19900201	AU 1989-38877	19890724
AU 619027	B2	19920116		
CA 1333771	A1	19950103	CA 1989-606620	19890725
ZA 8905710	A	19900425	ZA 1989-5710	19890727
HU 52378	A2	19900728	HU 1989-3821	19890727
HU 206827	B	19930128		
IL 91138	A1	19941021	IL 1989-91138	19890727
JP 02088521	A2	19900328	JP 1989-194417	19890728
JP 2848634	B2	19990120		
US 5369119	A	19941129	US 1993-26210	19930302
I DE 1988-3825667		19880728		
DE 1988-3844655		19880728		
US 1989-385920		19890727		
US 1990-617301		19901120		
US 1991-759204		19910911		

Imexon is an immunosuppressant which selectively suppresses B-lymphocyte activation and can be used in the treatment of B-cell or plasma cell leukemias or neoplasias. Thus, **imexon** inhibited the proliferation of stimulated human B-lymphocytes in vitro and inhibited the growth of methylcholanthrene-induced fibrosarcoma cells. It was also active against autoimmune diseases and infection with Rauscher leukemia virus.

ANSWER 20 OF 22 CAPLUS COPYRIGHT 2003 ACS
1978:164124 CAPLUS
88:164124
Experim ntal investigations on increased resistance to Candida albicans and Staphylococcus aureus Smith infections following 4-imino-1,4-diazobicyclo[3.1.0]hexane-2-one BM 06.002 (prop. INN **imexon**) treatment in mice
Ziegler, A. E.; Bicker, U.; Hebold, G.
Dep. Immunostimul., Boehringer Mannheim G.m.b.H., Mannheim, Fed. Rep. Ger.
Experimentelle Pathologie (1967-1980) (1977), 14(6), 321-7
CODEN: EXPTAX; ISSN: 0014-4908
Journal
English
BM 06.002 (I) [59643-91-3] increased the resistance of mice to exptl. induced chronic infection with C. albicans. Furthermore, I led to increased resistance in the case of exptl. induced infection with S.

aureus when a subtherapeutic dose of sulfadiazine was applied. In mice immunosuppressively pretreated with hydrocortisone, I initiated the restoration of the immune response.

ANSWER 21 OF 22 CAPLUS COPYRIGHT 2003 ACS
1978:99172 CAPLUS
88:99172
Experimental studies on the stimulation of cell-mediated immunoreactivity using 4-imino-1,3-diazabicyclo(3.1.0)hexan-2-one (BM 06.002, prop. INN **Imexon**)
Bicker, U.; Hebold, G.
Abt. Immunstimulation, Boehringer Mannheim G.m.b.H., Mannheim, Fed. Rep. Ger.
Oesterreichische Zeitschrift fuer Onkologie (1977), 4(2-3), 55-6
CODEN: OZOKAN; ISSN: 0377-2004
Journal
German
BM 06002 (**Imexon**) (I) [59643-91-3] amplified cell-mediated immunoreactivity in mice, as measured by the increase in the delayed-type hypersensitivity reaction (paw edema) to a booster shot of sheep erythrocyte. Doses of 2.5 and 25 mg/kg (i.v., on days, 0, 1, and 2 of the 1st immunization) were more effective than a dose of 250 mg/kg, and the clearest response was at 24 h after the booster immunization. An increase in both T-cell and macrophage function may be the mechanism of I action.

ANSWER 22 OF 22 CAPLUS COPYRIGHT 2003 ACS
1978:15884 CAPLUS
88:15884
Cancerostatic action of the immune-stimulating compound 4-imino-1,3-diazabicyclo-(3,1,0)-hexan-2-one, BM 06 002, (proposed inn **imexon**) on various transplantation tumors
Bicker, U.; Hebold, G.
Boehringer Mannheim G.m.b.H., Mannheim, Fed. Rep. Ger.
IRCS Medical Science: Library Compendium (1977), 5(9), 428
CODEN: IRLCDZ; ISSN: 0305-6651
Journal
English
BM 06002 (I [59643-91-3] (5 mg/kg, i.v.) given to mice had an antitumor activity against Friend virus leukemia, whereas cyclophosphamide (125 mg/kg, i.v.) had only a slight activity. I injected i.v. at 125 mg/kg into mice showed only a slight effect on Ehrlich ascites carcinoma in mice. I given orally to rats at this dose showed a clear cancerostatic effect on Walker carcinosarcoma.

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ST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
AL ESTIMATED COST	77.75	85.37

SCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
SUBSCRIBER PRICE	-14.97	-15.62

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